IN THE CLAIMS

The following claims have been canceled and added (see accompanying papers of new claims pursuant to 37 C.F.R. § 1.121(c)):

Claims 27, 32-33, and 39-45 have been canceled.

Claims 46-49 have been added.

REMARKS

The claims as amended herein are fully supported by the application as originally filed. No new matter has been added. Claims 46-49 are pending.

Applicants thank the Examiner for granting an interview on August 15, 2001 and appreciate the courtesies extended therein.

In the non-final office action of May 31, 2001 (Paper no. 22), the Examiner set forth the following rejections.

Claim Rejection under 35 U.S.C § 102

Claims 27, 32-33, and 39-45 were rejected under 35 U.S.C. § 102(b) as being anticipated by Wang, Ning, and Tanuma (AB and AC). Specifically, the Examiner asserted that (1) Wang teaches a method of diabetes comprising administering ginseng to the patient, and (2) Ning teaches a method of treatment of ischemia comprising administering ginseng to the patient. The Examiner also noted that Tanuma teaches that ginseng hot water extract "containing the lignin glycoside herein. Therefore the claimed method herein read on the method taught by Wang and Ning." (Citations omitted.)

Applicants disagree that Wang, Ning, and Tanuma (AB and AC) anticipate claims 27, 32-33, and 39-45. Notwithstanding such disagreement, applicants have withdrawn such claims from current consideration, thereby mooting the Examiner's rejection. With respect to new claims 46-

49, applicants note that Wang, Ning, and Tanuma do not disclose a method whereby therapeutically effective amounts of poly(ADP-ribose)glycohydrolase (PARG) inhibitors are used to treat neural or cardiac tissue damage resulting from a disease or condition. In particular, Wang and Ning do not disclose therapeutically effective amounts of a PARG inhibitor, let alone a PARG inhibitor that is used in a method for treating neural or cardiac tissue damage resulting from a disease or condition. The claims do not read on these references. A 35 U.S.C. § 102 rejection is not warranted.

In the Action the applicants' attention was directed to In re Swinehart, which was cited to support the Examiner's comment "that mode of action elucidation does not impart patentable moment to otherwise old and obvious subject matter." Applicants respectfully urge the Examiner to reconsider. New claims 46-49 are not claiming the old "thing" (e.g., lignin glycoside, which was mentioned in the canceled claims but not in the new claims) referred to in In re Swinehart on the basis of newly discovered properties or functions. Rather, applicants are claiming novel and possibly old compounds (i.e., PARG inhibitors) that are used in novel methods of treating neural or cardiac tissue damage resulting from a disease or condition. Such claims are well recognized as patentable subject matter. 35 U.S.C. § 100(b); In re Schoenwald, 964 F.2d 1122, 22 U.S.P.Q.2d 1671 (Fed. Cir. 1992); Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861, 875, 228 U.S.P.Q. 90, 99 (Fed. Cir. 1985) ("Even if a composition is old, a process using a known composition in a new and unobvious way may be patentable.").

Claim Rejection under 35 U.S.C § 103(a)

Claims 27, 32-33, and 39-44 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Tanuma (AB and AC) in view of both Wielckens et al. and Wachsman. In

particular the Examiner noted (in pages 3-5 of the Action) the detailed properties of lignin glycoside, a known PARG inhibitor, which is described in Tanuma as an anti-cancer agent.

The Examiner also asserted that Wachsman teaches that an inhibitor of poly(ADP-ribose)glycohydrolase will retard apoptosis, and that the depletion of intracellular NAD will result in the depletion of cellular energy. In addition, the Examiner stated that Wielckens et al. teach that the depletion of NAD is caused by drastic stimulation of poly(ADP-ribose) turnover, which is due to the high activity of both poly(ADP-ribose)polymerase and poly(ADP-ribose)glycohydrolase. (Citations omitted.)

The Examiner then concluded that is would have been prima facie obvious to a person of ordinary skill in the art to employ an inhibitor of poly(ADP-ribose)glycohydrolase (Tanuma) for treating or preventing diseases or conditions related to apoptosis (Wachsman) or for decreasing cellular energy depletion (Wielckens et al.).

Applicants respectfully disagree with the Examiner's conclusions regarding Tanuma, Wachsman, and Wielckens et al. When read as a whole, one of ordinary skill in the art would not have been motivated to combine Tanuma, in view of Wachsman and Wielckens et al., to suggest *with a reasonable expectation of success* that inhibitors of poly(ADP-ribose)glycohydrolase would likely retard apoptosis. A prior art reference must be considered in its entirety, as a whole invention, including portions that would lead away from the claimed invention.

When read as a whole, Wachsman does no more than offer an unsubstantiated guess that poly(ADP-ribose)glycohydrolase might—along with other enzymes—retard apoptosis. There is no experimental data (intracellular or otherwise) or specific guidance in Wachsman to support its guess that a chemical inhibitor of poly(ADP-ribose)glycohydrolase might retard apoptosis.

While obviousness does not require absolute predictability, at least some degree of predictability is required. Wachsman offers one of ordinary skill in the art no such predictability.

Moreover, the citation of Wachsman appears to utilize the long-rejected "obvious to try" standard. A classic improper "obvious to try" scenario arises when what is "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. Wachsman offers a singular statement with regard to apoptosis—with absolutely no experimentation or specific guidance in support. Such reliance on Wachsman improperly applies the "obvious to try" standard.

The deficiencies of Wachsman are prominently illustrated in a recent article by Swanson et al., where the authors report "results [of] the *first evidence* that PARG inhibitors could be used to prevent oxidative cell death." Swanson et al., *Neuropharmacology*, 11, 1385-1388 (2000) (see abstract and pg. 1387) (provided to the Examiner during a previous interview) (emphasis added). Thus, according to Dr. Swanson—one of the leading PARG researchers—the first evidence of PARG inhibitors being used to prevent cell death was published in May of 2000. Such evidence is strongly persuasive that Wachsman does not provide one of ordinary skill in the art the motivation to use PARG inhibitors to prevent cell damage or death due to apoptosis.

Notwithstanding such disagreement with respect to claims 27, 32-33, and 39-44, applicants have withdrawn such claims from consideration in order to facilitate the immediate prosecution of pending claims 46-49, thereby mooting the Examiner's rejection. With respect to new claims 46-49, applicants believe that the Examiner's stated teachings of Tanuma's PARG inhibiting lignin glycosides in view of Wielckens et al. poly(ADP-ribose) turnover and Wachsman's apoptosis mention do not teach or begin to fairly suggest claims to a method of

treating neural or cardiac tissue damage resulting from a disease or condition with PARG inhibitors. Among these references there is no teaching of neural or cardiac tissue damage resulting from the diseases or conditions claimed herein. One of ordinary skill in the art would not be motivated to combine Tanuma, in view of Wielckens et al. and Wachsman, to arrive at the subject matter of the pending claims. Applicants reject that this obviousness rejection be removed in light of pending claims 46-49 and argument hereto.

Second Claim Rejection under 35 U.S.C. § 103(a)

Claims 27, 32-33, and 39-44 were also rejected under 35 U.S.C. § 103(a) as being unpatentable over Wang or Ning in view of Tanuma (AB and AC).

Applicants disagree with the Examiner's conclusions but have withdrawn the rejected claims in order to facilitate the prosecution of pending claims 46-49, thereby mooting the Examiner's rejection. In view of the pending claims, applicants note that neither Wang nor Ning teach methods of treatment administering therapeutically effective levels of a PARG inhibitor (whether it be lignin glycoside or another PARG inhibitor) for the treatment of neural or cardiac tissue damage resulting from a disease or condition. Moreover, the Examiner explicitly notes that Tanuma only teaches certain uses of lignin glycoside (see Action, pgs. 3-4). These uses are not directed to the claimed method of treating neural or cardiac tissue damage resulting from a disease or condition with a PARG inhibitor. Applicants respectfully request that the Examiner withdraw this obviousness rejection in view of new claims 46-49.

In view of the new claims and foregoing argument, applicants submit that there is no basis for applying the previous rejections and observations to the pending claims. Accordingly, applicants believe the claims are in condition for immediate allowance and applicants earnestly solicit from the Examiner early notice of such favorable action.

Should the Examiner have any questions or believe a personal or telephonic interview may be in order, the Examiner is invited to contact the undersigned.

Respectfully submitted,

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